

REMARKS

Entry of this amendment and reconsideration of the subject application in view thereof are respectfully requested.

I. Claim Status

Claims 1-15 are pending in the application. These claims have been rejected. Claim 15 has been amended to overcome the objection. No new matter is added.

II. Claim Objections

The Examiner has objected to Claim 15 for "[t]he claim is independent, without any limitation of what the process is for." Applicant believes that this objection has been overcome in view of the amended claim 15 herein. Reconsideration is respectfully requested.

III. Rejections Under 35 U.S.C. § 103

Claims 1-15 stood rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 95 10514 ("D1"), Iwasaki et al., 1999, Chemical And Pharmaceutical Bulletin, JP (11-1999), Vol.42, pages 2285-2290 ("D2") Sejas et al., 1998, Tetrahedron, 44:6197-6200 ("D3") WO-A-9631478 ("D4"), EP 0,208,855 ("D5"), EP 0,152,897 ("D6"), US 4,659,716 ("D7"), or HU 194,864 ("D8") independently. This rejection is respectfully traversed and believed to be overcome in view of the following discussion:

Claim 1 is an independent claim, which is a process for the production of Desloratadine by "reacting loratadine with neat alcohol in presence of inorganic base, and isolating the title compound in crystalline form by conventional methods on addition of excess water."

The *Graham v. John Deere Co. of Kansas City*, 86 S. Ct. 684 (1966) factors control an obviousness inquiry. Those factors are: 1) "the scope and content of the prior art"; 2) the "differences between the prior art and the claims"; 3) "the level of ordinary skill in the pertinent art"; and 4) objective evidence of nonobviousness. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, at 1734 (2007) (quoting *Graham*, 383 U.S. at 17-18).

The Examiner admits that the cited prior art references, which disclose the process of

making Desloratadine (DCL) from loratadine in the presence of aqueous alcohol, do not disclose the use of neat alcohol in the process. The cited references also do not disclose isolating the title compound in crystalline form by conventional methods on addition of excess water. The Examiner seems to side step this fact.

The Examiner concludes that it is *prima facie* obvious for a chemist to modify the process of the prior art because (i) there is motivation to use neat alcohols in place of aqueous alcohol to make reactions faster and efficient (citing Peon et al., 2002, J. Am. Chem. Soc. 124:6428-6438 ("Peon")) and also, (ii) to a synthetic chemist, it would be within the scope of routine experimentation to try a neat solvent. Applicant respectfully traverses.

In order to establish a *prima facie* case of unpatentability in chemical cases, a showing that the "prior art would have suggested making the specific modifications necessary to achieve the claimed invention" is also required. *In re Deuel*, 51 F.3d 1552, 1558 (Fed. Cir. 1995). While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test in an obviousness analysis, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. *KSR*, 127 S. Ct. at 1731. Further, the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." *Id.* As long as the test is not applied as a "rigid and mandatory" formula, that test can provide "helpful insight" to an obviousness inquiry. *Id.* Thus, in chemical cases, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound.

Applicant respectfully points out that the rejection on obviousness grounds cannot be sustained by mere conclusory statements (made on page 4 of the Office Action) that "fuel cell customarily use neat solvents . . . and to a chemist it would be within the scope of routine experimentation to try a neat solvent, as changing solvents and experimental conditions is something a chemist routinely tries to modify a process." Instead, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F. 3d 977 (Fed. Cir. 2006). The Examiner has not provided a

sufficient reason or explicit analysis of why the cited prior art references should be modified so as to arrive at the claimed invention.

If anything, there is evidence to the contrary. Specifically, a clear pattern exists in the art for producing DCL by reacting loratadine with an aqueous alcohol and/or non-alcoholic solvents as evidenced by a number of references cited by the Examiner. The Peon reference concerns a study of proton transfer reactions between neat alcohol solvents and diphenylcarbene and reports experimental data on the rate of protonation of diphenylcarbene in singlet state. Peon has nothing to do with a process of making Desloratadine (DCL) from loratadine in the presence of neat alcohol, and it does not even remotely suggest DCL in pure crystalline form can be obtained upon addition of excess water to the reaction mixture.

A person of ordinary skill in the art, or a chemist, having common sense at the time of the invention would not have reasonably looked to neat alcohols and their effect on the rate of protonation of diphenylcarbene in singlet state to solve a problem already solved by the eight prior art references cited by the Examiner. Further, a person of ordinary skill in the art, or a chemist having common sense cannot arrive at the claimed invention simply by embedding a neat alcohol into a DCL production process in the manner suggested by the Examiner. The claimed process also requires a step of "isolating the title compound in crystalline form by conventional methods on addition of excess water."

The Examiner states on page 4 of the Office Action that "Applicants in their specification do not have a side by side comparison to show what and to what extent the improvement is . . . Applicants specification fails to show what the improvement is." Applicant respectfully disagrees and submits that the background information at pages 2-4 of the specification describes how DCL is made by the prior art processes. For example, in pertinent part, it describes that

"[i]t can be seen that the existing processes either relate to treating azatadine with cyanogen bromide followed by acid hydrolysis & neutralization or relate to alkali or acid hydrolysis of loratadine using alkali metal hydroxide with aqueous alcohol. The processes involve refluxing for a longer period ranging from 24 to 66 hrs or even more upto 4 days. The product is invariably coloured and needs further purification.

Then the Summary of the invention and detailed description of the invention describe what the improvement is. For example, it describes that:

“the process of the present invention is unexpectedly advantageous for the commercial scale production of the title compound with high yield, high purity, and low value residual solvent . . . the present invention provides an improved process for the production of Desloratadine which comprises, reacting loratadine with neat alcohol in presence of inorganic base, and isolating the title compound in crystalline form by conventional methods on addition of excess water . . . it is observed that the loratadine when heated with neat MeOH and NaOH for about 1 to 6 hrs produces DCL that can be isolated easily by adding excess of water in pure crystalline form with high yield. The product obtained does not develop any colour on storage and meets all ICH requirements, GMP requirements & health registration requirements. Thus the process of the present invention is easy to operate, environment friendly economic and useful for commercial production.”

See, the specification at page 5, line 2 through page 7, line 6. Tables 1 and 3 provide actual data on quality results. One skilled in the art would know what the improvement is compared to the prior art processes by reading the specification. A “side by side comparison” is not a requirement to prove non-obviousness of an invention.

As such, there is no suggestion to modify the teachings and suggestions of D1-D8, as advanced by the Examiner, except from using Applicant’s invention as a template through a hindsight reconstruction of Applicant’s claims. The Examiner’s reliance on the routine nature of the data gathering required to arrive at Applicant’s discovery, after its existence is known, is believed to overlook the requirements of 35 U.S.C. § 103. More specifically, the Examiner has impermissibly used the instant claims as a guide or roadmap in formulating the rejection. Therefore, the Examiner’s rejection is believed to stand in error.

In view of the foregoing, Applicant respectfully submits that the Examiner has not established a *prima facie* case of obviousness of the independent claim 1 under 35 U.S.C. § 103(a). Even if *prima facie* obviousness has been established, which it has not, it is urged that the cited art nonetheless fails to render the present invention obvious under a proper § 103 analysis, as the proper suggestions and motivations are lacking in the cited reference.

Applicant also submits that the Examiner has not established a *prima facie* case of obviousness of dependent claims 2-15 under 35 U.S.C. § 103(a). In particular, rejected dependent claims 2-15, by virtue of their dependency from the corresponding independent claim

Serial No.: 10/529,008

1 are similarly considered by Applicant to patentably define themselves over the cited reference. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

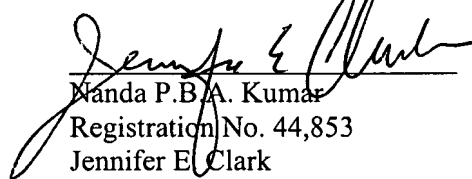
IV. Conclusion

Applicant believes this response to be a full and complete response to the Office Action. Accordingly, favorable reconsideration in view of this response and allowance of all of the pending claims are earnestly solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

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Respectfully submitted



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